REMARKS

Entry of this Amendment is proper under 37 C.F.R. §1.116 because the Amendment places the application in condition for allowance for the reasons discussed herein; and does not raise any new issues requiring further search and/or consideration as the amendments amplify issues previously discussed throughout prosecution. Entry of the Amendment is thus respectfully requested.

Claims 1-57 are currently pending. Claims 17-33, 35, 36, and 38-57 stand withdrawn. Claims 2, 4, 34, and 37 are canceled herein without prejudice or disclaimer thereto. Applicants reserve the right to file at least one continuation application directed to any subject matter canceled herein.

Claims 1, 5, and 11-14 are amended herein. Basis for these amendments may be found throughout the specification and claims as-filed, especially at page 4, first paragraph and page 8, line 32 to page 9, line 2. Thus, no new matter is submitted herewith.

Applicants note with appreciation that the objections to claim 2 under 35 U.S.C. §112, second paragraph, and claims 1-6 and 16 under 35 U.S.C. §101 are withdrawn.

Applicants thank Examiner Helms for his suggestion via telephone that he and/or Examiner Tungaturthi would contact Applicants following the filing of the present Amendment, if suggestions may advance prosecution or gain allowance.

Rejections under 35 USC § 112, second paragraph

Claims 1-16, 34, and 37 stand rejected under 35 U.S.C. §112, second paragraph, as purportedly indefinite.

The claims stand rejected for the recitation of "derivative". In the interest of expediting prosecution, the term derivative has been removed from the claims by way of the present Amendment. Thus, this rejection is moot.

Claim 1 stands rejected for the recitation of "similar unique binding properties". In the interest of expediting prosecution, claim 1 is amended herein to remove this phase, and thus rejection is moot.

Claim 5 stands rejected as purportedly indefinite for reciting "sequences have an identify of at least 84%". Claim 5 is amended herein to recite " the sequences of

the antibody or fragment thereof have an identity of at least 84% to corresponding sequences of human origin and complementary determining region (CDR) sequences of claim 1", to further clarify that it is the CDR sequences which have an identity of at least 84% to corresponding sequences of human origin.

Claims 11-14 stand rejected for reciting "changed" because it is purportedly unclear how the antibody has been "changed". Claims 11-14 are amended herein to recite that the antibodies are genetically changed.

Claim 15 stands rejected for the recitation of "other binding structures" as it is purportedly unclear if they bind the same antigen as the unlabeled antibody. Applicants submit that this phrase is well known in the art as referring to other antibodies or binding entities.

Claim 1 stands rejected as purportedly indefinite for reciting "subpopulation of normal human gastrointestinal epithelial cells". In the interest of expediting prosecution, this phase has been removed herein from claim 1.

In light of the above, Applicants request that the rejections under 35 U.S.C. §112, second paragraph, be withdrawn.

Claim Rejections under 35 U.S.C. §112, first paragraph

Claims 34 and 37 stand rejected under 35 U.S.C. §112, first paragraph. In the interest of expediting prosecution, and without acquiescing in the rejection, claims 34 and 37 are canceled herein without prejudice or disclaimer thereto. Thus, this rejection is moot.

Claim Rejections under 35 U.S.C. §§102 and 103

Claims 1, 2, 7, 8, 9, 34 and 37 stand rejected under 35 U.S.C. §102(b) as purportedly anticipated by Fernsten et al. (*Cancer Research* 51:926-934, 1991) ("Fernsten"). Applicants traverse.

To anticipate a claimed invention under §102, a reference must teach each and every element of the claimed invention. *See Lindeman Machinenfabrik GmbH v. American Hoist and Derrick Company*, 221 USPQ 481, 485 (Fed. Cir. 1984). Fernsten does not recite each element of the present invention, as amended herein.

Independent claim 1 is amended herein to recite that the antibody or fragment at issue has specific CDR sequences, as also listed in the claim. Fernsten fails to recite these CDR sequences. Thus, Fernsten fails to recite each element of the present invention.

Claims 1, 2, 7, 16, 34, and 37, stand rejected under 35 U.S.C. §102(b) purportedly as being anticipated by Quaranta et al. (U.S. Patent No. 5,320,942) ("Quaranta"). As noted, claim 1 now recites that the antibody or fragment thereof has specific CDR sequences. Quaranta fails to disclose these CDR sequences. Thus, Quaranta fails to recite each element of the present invention.

Claims 1, 2, 4-15, 34, and 37, stand rejected under 35 U.S.C. §103(a) as purportedly unpatentable over Fernsten in view of Queen et al. (U.S. Patent No. 6,180,370) ("Queen").

As set forth in MPEP §2142, in order to establish a prima facie case of obviousness, three criteria must be met: (1) there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings, (2) there must be a reasonable expectation of success, and (3) the prior art references must teach or suggest all the claim limitations.

As noted, Fernsten fails to recite each element of the present claims and fails to recite the presently claimed CDRs. Queen fails to remedy these deficiencies, as Queen is directed to the production of humanized antibodies that are non-immunogenic in humans. However, Queen does not recite the CDRs of the present claims. Thus, not only do Fernsten and Queen fail to recite each element of the present invention, these two references in combination do not provide a motivation to modify or an expectation of success.

It is further significant that the cited references fail to recite the presently claimed CDRs. The present invention provides technology which produces an antibody with unique and advantageous properties. These properties are embodied in the CDR sequences of the present invention.

Specifically, the A3 antibody provides the following particular advantages. The A3 antibody displays a reactivity pattern as determined by immunohistochemistry on human tumor and normal tissues. A3 recognizes epitopes

homogenously expressed in colon and pancreatic carcinomas while having restricted reactivity to epithelial normal tissues such as of the lung and kidney. The most prominent normal tissue reactivity of the A3 has been shown in staining of normal colon epithelium. Weak staining was also detected in small ducts of the pancreas and bile ducts of the liver as well as of substructures in small bowel epithelial.

A functional test of superantigen antibody-dependent cellular cytotoxicity towards Colo 205 tumor cells was performed for A3 scFv fused to superantigen SEA(D227A). The test demonstrated efficient T-cell-mediated killing of colon cancer cells coated with A3 scFv fused to the low MHC class II binding superantigen mutant SEA(D227A).

In addition, the present invention uses phage display and subtractive tissue-based phage selection to generate antibodies. This is advantageous, because tissue sections are a biological material that provides accessibility to a broad spectrum of biological molecules in their native tissue expressed form. This technology provides access to molecular targets selectively expressed in disease states such as cancer. Thus, is it possible to generate antibodies targeting new potential tumor antigens.

The above, and disclosed, properties of the A3 antibody make it very useful for immunotherapy use in pancreatic and colon cancer. These advantages are conferred by the CDRs of the antibody recited in the present claims. These CDRs and resulting advantages are not disclosed in the cited references, taken alone or in combination.

Claims 1, 2, 4-16, 34, 37, stand rejected under 35 U.S.C. §103(a) as being unpatentable over Quaranta in further view of Queen. Applicants traverse. As noted, claim 1 now recites that the antibody or fragment thereof has specific CDR sequences. Quaranta fails to disclose these CDR sequences. Queen fails to remedy these deficiencies, as Queen does not recite the CDRs of the present claims. Thus, not only do Quarenta and Queen fail to recite each element of the present invention, these two references in combination do not provide an expectation of success.

Claims 1-9, 11, 14-16, 34, and 37, stand rejected under 35 U.S.C. §103(a) as being unpatentable over Quaranta in view of Anderson et al. (U.S. Patent No.

6,113,898) ("Anderson"). Anderson fails to remedy the deficiencies of Quarenta, as Anderson merely discloses Anderson discloses a method of phage selection where the phage library is screened for antibodies abilities to bind to soluble purified human B7, B7.1 or B7.2 antigen coated plates. Anderson does not disclose the CDRs of the present invention, and fails to provide a phage display method for positive and subtractive selection of phage antibodies employing intact cells as the antigen source.

In light of the above, Applicants request that the rejections under 35 U.S.C. §§102 and 103 be withdrawn.

CONCLUSION

In the event that there are any questions relating to this application, it would be appreciated if the Examiner would telephone the undersigned concerning such questions so that prosecution of this application may be expedited.

The Director is hereby authorized to charge any appropriate fees that may be required by this paper, and to credit any overpayment, to Deposit Account No. 02-4800.

Respectfully submitted,

BUCHANAN INGERSOLL PC
(INCLUDING ATTORNEYS FROM BURNS DOANE SWECKER & MATHIS)

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